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Research Article

Comparison of Maternal Serum Ferritin and C-reactive protein Levels in the Diagnosis of Preterm Labor

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Abstract

Background: Preterm labor remains a principal cause of neonatal morbidity and mortality globally, with mostly high incidence in low- and middle-income countries like Bangladesh and across the Indian subcontinent. Despite worldwide efforts, early identification of preterm labor remains a challenge, highlighting the necessity for consistent, reachable biomarkers to recover maternal and neonatal outcomes in these areas.

Aim: To establish the comparison between maternal serum ferritin and C-reactive protein (CRP) levels in preterm labor.

Methods: A case-control study was conducted at the Department of Obstetrics and Gynecology, Bangladesh Medical University, from June 2022 to May 2023. A total of 130 pregnant women in labor (65 preterm, 65 full term) were registered using non-probability sampling technique. Serum ferritin and CRP levels were measured using Microparticle Enzyme Immunoassay (MEIA) and Particle Enhanced Turbidimetric Immunoassay (PETIA), methods, correspondingly. Data were analyzed with SPSS v26, $p < 0.05$ measured statistically significant. Ethical approval and informed consent were obtained.

Results: Maternal serum ferritin levels were significantly lower in preterm cases compared to full-term controls (mean ± SD: 1.98 ± 0.12 vs. 2.00 ± 0.00 ng/ml, $p = 0.044$). ROC curve analysis for ferritin at a cutoff ≤26 ng/ml presented a sensitivity of 60.1%, specificity of 84.6%, and overall accuracy of 90.0%. In contrast, CRP levels were significantly raised in the preterm group, with 81.5% display increased CRP compared to none in the full-term group ($p < 0.001$). ROC curve for CRP shown excellent power, confirming its higher predictive value for preterm labor.

Conclusion: CRP displayed significantly developed diagnostic correctness than serum ferritin in finding preterm labor. Its strong sensitivity and specificity support its potential as a valuable early marker in clinical assessment. Incorporating CRP testing may advance early detection and managing of preterm labor risk.

Keywords: Preterm Labor; C-Reactive Protein; Serum Ferritin; Biomarkers; Maternal Health

Introduction

Preterm labor (PTL), defined as childbirth happening before 37 weeks of gestation, remains the top cause of neonatal morbidity and mortality globally, contributing to around 35% of neonatal deaths globally [1,2]. A projected 15 million preterm births occur yearly, with an uneven burden in low- and middle-income states [3,4]. Several maternal, fetal, and environmental issues have been concerned, yet early identification of women at risk remains a main challenge [5].

Inflammatory methods are vital to the pathophysiology of spontaneous preterm labor. The maternal immune reply, especially activation of inflammatory markers such as CRP and ferritin, is often experiential in women who go into preterm labor [6,7]. CRP, an acute-phase protein synthesized by the liver in response to interleukin-6, has been anticipated as a non-invasive biomarker for noticing intrauterine inflammation and infection [8,9]. Raised maternal CRP levels have been stated in association with subclinical chorioamnionitis and opposing pregnancy outcomes [10,11].

Serum ferritin, a major iron storage protein, also acts as an acute-phase reactant. Outside iron metabolism, ferritin levels increase in retort to systemic inflammation, possibly helping as an early pointer of infectious or inflammatory triggers of PTL [12,13]. Some studies have noted high ferritin concentrations in women with preterm premature rupture of membranes (PPROM) and PTL, supportive its prognostic significance [14,15].

Yet, the diagnostic accurateness of these markers differs. Whereas some reports display high sensitivity and specificity of CRP and ferritin in expecting preterm delivery, others statement unreliable results, expected due to heterogeneity in population characteristics, gestational age windows, and assay methods [16,17]. For example, a study by Shalal et al. found no significant association between CRP/ferritin levels and intra-amniotic infection in PPROM cases, while Valappil et al. confirmed raised ferritin in such conditions [18,19].

Furthermore, an increasing body of literature supports using ROC curve analysis to improve cutoff values and recover the predictive accuracy of these biomarkers [20,21]. Yet, despite these progressions, the comparative diagnostic value of maternal serum ferritin and CRP in spontaneous preterm labor remains inefficiently addressed in the literature.

This study aims to fill this gap by comparison maternal serum ferritin and CRP levels in women with preterm and full-term labor, and to evaluate their predictive rate with sensitivity, specificity, and ROC investigation.

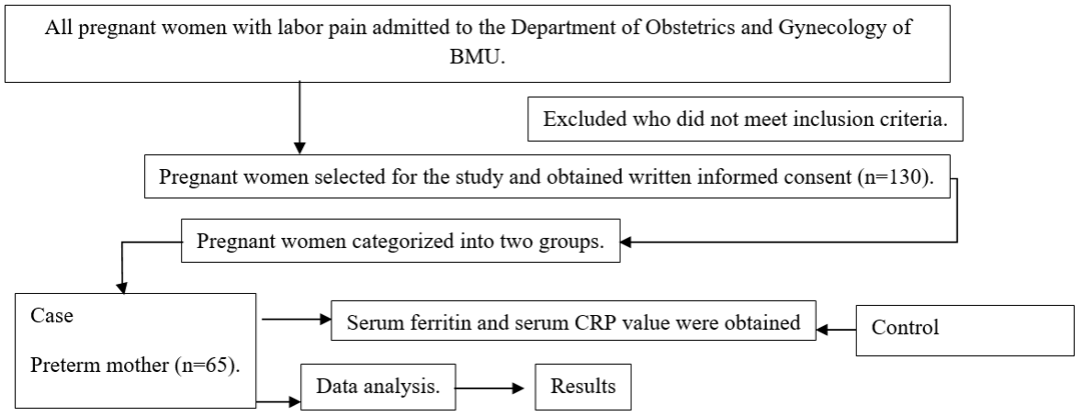
Methods

This case-control study was conducted in the Department of Obstetrics and Gynaecology at Bangladesh Medical University from June 1, 2022, to May 31, 2023. A total of 130 pregnant women acknowledged with labor pain were join up through non-probability suitable sampling, including 65 with preterm labor and 65 with term. Qualified participants were aged <20 to >30+ years with pregnancies. Women with anemia (hemoglobin <10.5 g/dL), chronic diseases, infections, pregnancy complications, or fetal anomalies were excluded.

After informed consent, demographic and obstetric data were collected, and gestational age was established by last menstrual period and early ultrasound. Almost 6 mL of venous blood was collected from each participant.

Statistical analysis was accomplished using SPSS version 26. Pearson correlation assessed associations with gestational age, and ROC curve with the Youden Index determined diagnostic cutoffs. A p-value <0.05 was measured significant. Ethical approval was taken from the Bangladesh Medical University Ethical Review Committee, and written informed consent was collected from all participants.

Study flow diagram



Results: In this comparative study of maternal serum biomarkers in preterm labor, 130 pregnant women were analyzed, among them 65 with preterm and 65 with full-term deliveries.

Serum ferritin (≤26-≥220 ng /ml)	n	Mean ± SD	t	*p*-value
Preterm	65	1.9846 ± 12403	4.000	.044
Full term	65	2.0000 ± .00000		

Table 1: Comparison between preterm and full term as regard Ferritin.

Table 1 shows maternal serum ferritin levels were significantly lower in the preterm labor group compared to the full-term group (mean ± SD: 1.98 ± 0.12 vs. 2.00 ± 0.00 ng/ml; t = 4.000, $p = 0.044$). This suggests a potential association between reduced ferritin levels and preterm labor.

At a serum ferritin cutoff value of ≤26 ng/ml, the ROC analysis demonstrated a sensitivity of 60.1% and a specificity of 84.6% for predicting preterm labor. The positive predictive value (PPV) was 76%, the negative predictive value (NPV) was 80%, and the overall accuracy reached 90.0%, indicating that ferritin is a moderately sensitive but highly specific marker for preterm labor prediction.

ROC curve in prediction of preterm labour as regard Ferritin					
Cut off	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
≤26	60.1	84.6	76	80	90.0

Table 2: The results derived from ROC curve show the accuracy of Ferritin by sensitivity (sens), specificity (spec) at cut off predictive value in prediction of preterm labour.

Table 3 displays a significant difference was observed in gestational age distribution and CRP levels between preterm and full-term groups ($p = .000$). All full-term cases had gestational ages >30 weeks, while the preterm group ranged below 30 weeks. Additionally, elevated CRP levels were found in 81.5% (53/65) of preterm cases versus none in the full-term group, suggesting a strong association between increased CRP and preterm labor.

Figure 1 shows the ROC curve for CRP levels in predicting preterm labor illustrates a strong diagnostic performance, with a clear separation between preterm and full-term outcomes. The curve

Gestational age	Preterm	Full term	p-Value
<20 Weeks	18	00	.000[f]
20-30 Weeks	47	00	
>30 Weeks	00	65	
CRP level			
Normal	12	65	.000[f]
Increased	53	00	
Total	**65**	65	130

Table 3: Comparison between preterm and full term as gestational age and CRP level.

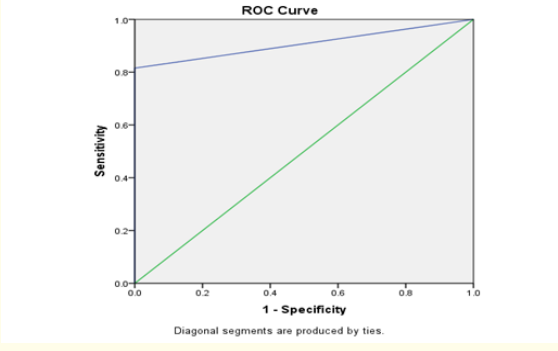


Figure 1: ROC curve for category of CRP level.

suggests that elevated CRP is a reliable predictor, with high sensitivity and specificity, supporting its role as a valuable inflammatory marker in identifying preterm labor risk.

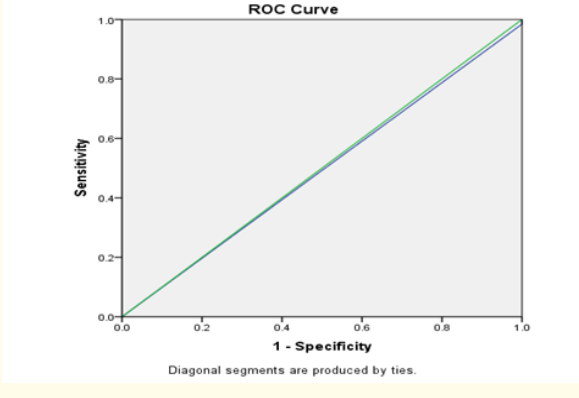


Figure 2: ROC curve for category of serum ferritin.

Figure 2 express the ROC curve for serum ferritin in predicting preterm labor shows a moderate diagnostic ability. The curve indicates that serum ferritin, at a cutoff of ≤26 ng/ml, provides good specificity with acceptable sensitivity, reinforcing its potential as a useful biomarker in identifying women at risk of preterm labor.

Discussion

This study aimed to compare the diagnostic performance of maternal serum ferritin and CRP levels in classifying preterm labor. The results revealed that while both biomarkers presented significant changes between preterm and full-term groups, CRP demonstrated stronger diagnostic value.

Higher levels of CRP were significantly related with preterm labor, with 81.5% of preterm cases presentingenlarged CRP levels associated to none in the full-term group. This thought aligns with earlier studies that highlighted the role of maternal systemic inflammation in the pathogenesis of spontaneous preterm birth, wherever CRP acts as an acute-phase reactant and a sensitive marker for infection or inflammation [7,12]. The high sensitivity and specificity of CRP, as established in ROC curve analysis, support its utility as a non-invasive, rapid diagnostic tool for early identification of preterm labor risk.

In contrast, ferritin levels, while statistically lower in preterm cases (p = 0.044), demonstrated moderate sensitivity 60.1% and higher specificity 84.6% at the ≤26 ng/ml threshold. Ferritin, an iron-storage protein, also acts as an acute-phase reactant and may

reproduce subclinical inflammation or iron metabolism disruption in pregnancy [13]. Nevertheless, the narrow variance in mean ferritin values between the groups in our study may bind its standalone predictive size, especially when associated to the robust performance of CRP.

The results are reliable with earlier literature signifying that inflammation and infection are key contributors to preterm birth, mainly through the activation of cytokine pathways that stimulate uterine contractility and cervical ripening [5,8]. Raised CRP levels are frequently reflective of intrauterine or systemic maternal inflammation, both of which are concerned in the early beginning of labor processes [15,16].

Gestational age distribution further maintained the biomarker data. All full-term cases surpassed 30 weeks, while preterm cases clustered below 30 weeks, with a notable subgroup under 20 weeks, highlighting the potential clinical utility of early CRP screening in high-risk pregnancies. These findings also align with the global burden of preterm birth as described in large-scale epidemiological studies [1].

While CRP appears to be a more reliable biomarker for diagnosing preterm labor, it is important to interpret these findings within a broader clinical context. Factors such as maternal infections, chronic inflammation, and concurrent medical conditions can influence CRP levels, which may reduce specificity in some populations. On the other hand, ferritin may still offer value when used alongside other inflammatory markers or in cases where iron deficiency complicates pregnancy outcomes [9,18].

Conclusion

This study demonstrates that maternal CRP levels are more reliable than serum ferritin in predicting preterm labor. While both biomarkers showed significant differences between preterm and term groups, CRP offered greater diagnostic sensitivity and specificity. These findings support the incorporation of CRP measurement into routine antenatal assessment, especially in high-risk pregnancies. However, further large-scale, prospective studies are needed to confirm these results and to evaluate the potential utility of combining CRP with other clinical and biochemical markers for improved prediction of preterm labor.

Declaration of Interest

The authors declare no competing interests.

Authors Contributions

Prof. Dr. Tripti Rani Das and Dr. Sabiha Islam conceptualized the study and designed the methodology. Farah Noor and Dr. Iffat Rahman contributed data management and statistical analysis. Dr. Shah Noor Sharmin, Dr. Jinat Fatema and Dr. Bidisha Chakma assisted in manuscript drafting and critical revisions. Prof. Dr. Tripti Rani Das and Dr. Tanzina Iveen Chowdhury supervised the research and provided final manuscript approval. All authors reviewed and approved the final version.

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